Ephrin-As are required for the topographic mapping but not laminar choice of physiologically distinct RGC types.

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Public Summary:
The vast number of neurons in the brain connect precisely to one another, with the axons of one neuron contacting the dendrites or other parts of many postsynaptic neurons. One of the puzzles that this complex "connectome" poses is how each neuron is correctly wired to its postsynaptic targets. There are many molecular cues that neurons use to connect to each other; in the visual system one family of cues are the Ephs and ephrins (receptors and ligands respectively) whose graded expression in the retina's output neurons and their target brain regions regions allow for the formation of topographic maps. We wondered whether each of the different subtypes of retinal output neurons (called retinal ganglion cells; RGCs) rely equally on this Eph/ephrin system to target their axons correctly. Furthermore, since each RGC subtypes send their axons to different layers of an early target center, we wondered whether they rely on each other to form their topographic maps in different layers or whether each RGC type forms a map independently of other types. We used a genetic mouse model in which several members of the ephrin fmaily were deleted to ask these questions. All RGC types that we looked at showed mistargeting when Eph/ephrin signaling was disturbed in this way, and misalignment between maps of different RGC types implies that each type forms a map somewhat independently of other types.

Scientific Abstract:
In the retinocollicular projection, the axons from functionally distinct retinal ganglion cell (RGC) types form synapses in a stereotypical manner along the superficial to deep axis of the superior colliculus (SC). Each lamina contains an orderly topographic map of the visual scene but different laminae receive inputs from distinct sets of RGCs, and inputs to each lamina are aligned with the others to integrate parallel streams of visual information. To determine the relationship between laminar organization and topography of physiologically defined RGC types, we used genetic and anatomical axon tracing techniques in wild type and ephrin-A mutant mice. We find that adjacent RGCs of the same physiological type can send axons to both ectopic and normal topographic locations, supporting a penetrance model for ephrin-A independent mapping cues. While the overall laminar organization in the SC is unaffected in ephrin-A2/A5 double mutant mice, analysis of the laminar locations of ectopic terminations shows that the topographic maps of different RGC types are misaligned. These data lend support to the hypothesis that the retinocollicular projection is a superimposition of a number of individual two-dimensional topographic maps that originate from specific types of RGCs, require ephrin-A signaling, and form independently of the other maps.